

**REMARKS**

**Amendments to the Specification**

The Title is amended again to indicate more clearly that the term "novel" has been deleted. The paragraph beginning on line 12 of page 28 is amended to clarify the date of submission of biological material and the address of the depository to which the submission was made. No new matter has been added.

**Claims**

Claim 35 is canceled, without prejudice or disclaimer. Applicants reserve the right to pursue this subject matter in a continuation application.

**Indefiniteness rejection of claim 36**

Applicants do not understand this rejection. The claim, does, indeed, recite positive steps: "cultivating" and "collecting." Furthermore, it is noted that the language of this claim closely parallels the language of claim 37 of granted USP 7,244,761, which is cited by the Examiner in an obvious-type double patenting rejection the Office Action of September 24, 2008.

Claim 37 of the issued patent is:

A process for producing the compound represented by formula [12], wherein the process comprises the steps of: 1) cultivating in a culture medium a compound-producing fungus which belongs to the genus *Penicillium*, which is *Penicillium* sp. SPF-3059 having accession number FERM BP-7663 to produce a compound of formula [12], [formula] wherein R<sup>1</sup> represents a hydrogen atom, a carboxyl group or an alkoxycarbonyl group, R<sup>2</sup> represents a hydrogen atom, a hydroxyl group or an acyloxy group, R<sup>4</sup> represents a hydrogen atom, a carboxyl group or an alkoxycarbonyl group and R<sup>5</sup> represents a hydrogen atom, a hydroxyl group or an acyloxy group; and 2) isolating the compound from the culture medium.

A skilled worker would presumably be aware of USP 7,244,761, and would presumably have understood the language in claim 37 of that issued patent. Therefore, the skilled worker would also understand the similar language in present claim 36. For at least the above reasons, the language in present claim 36 is clear, and not indefinite. Applicants request that the rejection be reconsidered and withdrawn

Enablement rejection of claim 35

Claim 35 has been canceled, thereby rendering the rejection moot.

Written description rejection of claim 36 (biological deposit)

As requested by the Examiner, Applicants point out that the deposition information is located at page 28, second paragraph of the section in the specification as filed entitled "Temperature range for growth." The passage indicates that

The strain was deposited to the International Patent Organism Depository of the National Institute of Advanced Industrial Science and Technology, an Independent Administrative Institution, Japan under the accession number FERM BP-7663 as the International Deposition Number under the Budapest Treaty on the international recognition of the deposit of microorganisms for the purpose of patent procedure.

Furthermore, a copy of the Depository Receipt and an English translation thereof were filed with the Amendment of April 30, 2008; and attorney Hobbs confirmed, over her signature and registration number, that during the pendency of the application access to the invention will be afforded to the Commissioner upon request; that upon the granting of a patent all restrictions upon availability to the public will be removed; that the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; that a test of the viability of the biological material at the time of the deposit was made; and that the deposit will be replaced if it should ever become inviable.

Per the request of the Examiner, the specification has been amended to clarify the date of the deposit and the address of the depository. Reconsideration and withdrawal of the rejection is requested.

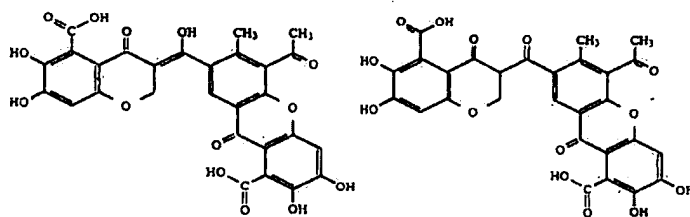
Obviousness rejection of claims 1, 10, 11, 13-16 and 36 over Masubuchi *et al.*, in view of Abrahart

Applicants respectfully disagree with the Examiner's rationale for rejecting these claims, for at least the following reasons:

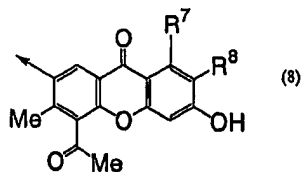
The Examiner appears not to have considered the arguments raised by Applicants in the Amendment filed April 30, 2008, and the two Supplemental Amendments, filed May 22, 2008

and June 6, 2008, *e.g.* the argument that the core structures of the group of compounds covered by the claims of the present application and the core of the compounds of cited reference Masubichi *et al.* (Xanthofulvin and its tautomer) are different. Such a difference between the cores is significant. These arguments are reiterated below. Masubichi *et al.* does not suggest or disclose the claimed invention. The secondary reference, Abrahart, does not remedy this deficiency. Therefore, for at least this reason, the combination of the cited references does not render the presently claimed compounds obvious.

The Examiner has taken the position that Masubuchi *et al.* discloses in column 1, lines 10-40 the following Xanthofulvin and tautomer thereof.

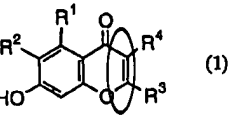
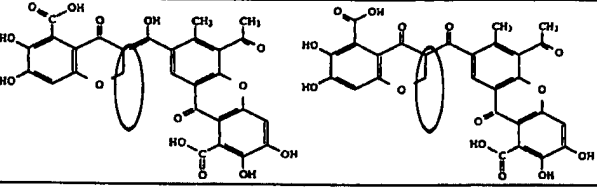


According to the Examiner, the above Xanthofulvin and tautomer thereof correspond to the compound of general formula (1) of the present application, wherein  $R^3$  is formula (8):



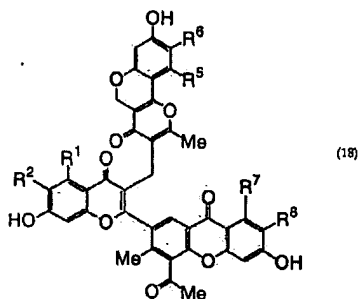
wherein  $R^7$  is a carboxyl group, and  $R^8$  is a hydroxyl group.

To reiterate the arguments presented in the Amendment filed on April 30, 2008 and the two Supplemental Amendments concerning the differences in the core structures of the claimed compounds and the compounds of the reference, the compounds of common general formula (1) of claim 1 of the present application have a double bond between the carbon atom bearing the  $R^3$  substituent and the carbon atom bearing the  $R^4$  substituent, whereas, by contrast, in Xanthofulvin and its tautomer, the corresponding part is bound by a single bond and not by a double bond. This difference is illustrated in the chemical formulae below, with the relevant portions circled for convenience.

The scope of the claims of the present application	Xanthofulvin and its tautomer
<p>General formula of Claim 1 :</p>  <p>(1)</p>	

As shown above, the core of the group of compounds covered by the claims of the present application and the core of Xanthofulvin and its tautomer are different. Such a difference between the cores is significant. *The compound of the present invention cannot be said to be an analogue of Xanthofulvin or its tautomer.*

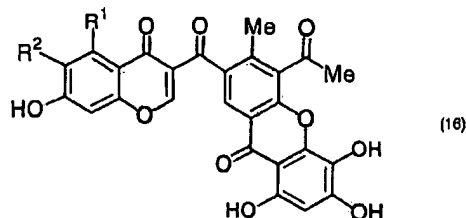
Furthermore, other elements of the structures of the claimed compounds are significantly different from those of the references. As was noted in the Amendment filed on April 30, 2008, the Examiner refers to the case where  $R^3$ =formula (8),  $R^7$ =carboxyl group, and  $R^8$ =hydroxyl group in general formula (1) of the present application. These requirements fall under Claim 1 [VII], and claims 14-15 of the present application. However, these claims also essentially require that " $R^4$ =formula (9)". These requirements all inclusive are represented by general formula (18):



As can be seen, the compounds within the scope of the claims of the present application with  $R^3$ =formula (8),  $R^7$ =carboxyl group, and  $R^8$ =hydroxyl group as referred to by the Examiner are *totally different* from Xanthofulvin and its tautomer in structure. Therefore, it is evident that Xanthofulvin and its tautomer are not included in the scope of the claims of the present invention.

Incidentally, if the Applicants were required to present the structural formula closest to that of the above Xanthofulvin and a tautomer thereof, claim 1 [V] and claims 10-11, represented

by formula (16), would be chosen:



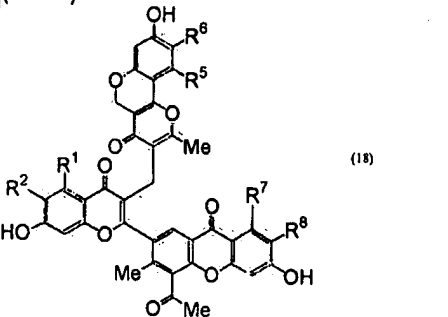
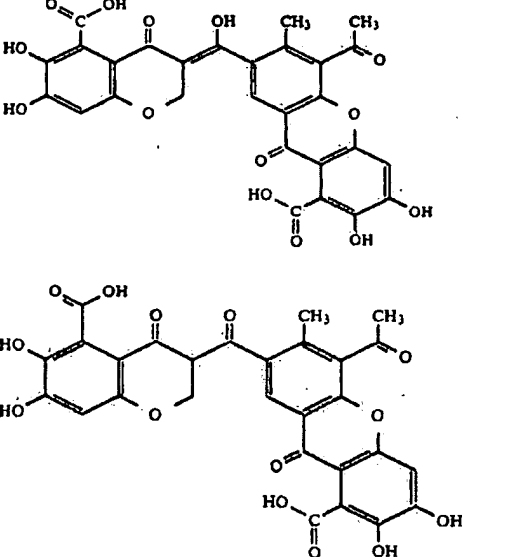
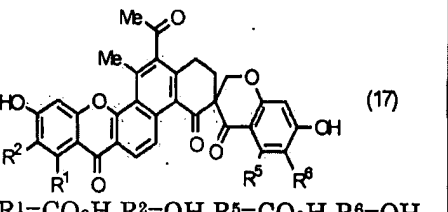
In this case, the Examiner's attention is called to the benzene ring of the terminal end of the tricyclic part. The substituents on this ring are limited to three hydroxyl groups. In the above Xanthofulvin and a tautomer thereof, the corresponding substituents on the benzene ring in the tricyclic part are two hydroxyl groups and one carboxyl group, and in addition, the sites of substitution are different. In this respect, the compounds in the scope of the claims of the present application are different from the above Xanthofulvin and a tautomer thereof. See the chemical formulae below, in which the relevant portions are circled for clarity. Applicants again emphasize that not only are the substituents on the benzene ring on the terminal side of the tricyclic moiety different, but the core structures are also different. From this, it is clear that the above Xanthofulvin and a tautomer thereof are not included in the scope of the claims of the present application.

The scope of the claims of the present application	Xanthofulvin and a tautomer thereof

It is noted that Claim 16 was previously canceled, so the rejection of this claim is moot.

As for dependent Claim 13, in addition to the difference in the core structure of this compound and the compound of the reference, it is clear from the following Table that the

compound of formula (17), whose requirements fall under Claim 13, is significantly different from the compound of the cited reference.

Dependent claims of the present application	Xanthofulvin and its tautomer
<p>(14-15)</p>  <p>(18)</p>	
<p>(13)</p>  <p>(17)</p> <p><math>R^1=CO_2H, R^2=OH, R^5=CO_2H, R^6=OH</math></p>	

Furthermore, Applicants respectfully disagree with the allegation by the Examiner (as Applicants understand it) that the Masubuchi *et al.* reference, in view of Abrahart, would render it obvious for a skilled worker to modify one of the presently claimed structures to generate Xanthofulvin or its tautomer. In the Office Action of September 4, 2008, on page 11, last paragraph of the rejection under 35 USC 103, the Examiner appears to allege that some of the "substituents on the phenyl ring of the xanthone moiety" of some of the claimed compounds would be obvious over Masubuchi *et al.*, in view of Abrahart, which is a page directed to "Dyes and their Intermediates." However, there appear to be some grammatical errors or omissions of words in the Office Action, and the meaning of the rejection is not clear. Clarification of this rejection is requested.

If the Examiner is alleging that xanthone is a known dye, that the substituents OH and COOH are known auxochromes on xanthone dyes, and that it thus would have been obvious to exchange these known substituents for one another on the xanthone moiety that is part of the presently claimed molecules, with predictable, expected results, applicants respectfully disagree.

For one thing, the Examiner has presented no support for his allegation that xanthone is a known dye, or that, in the context of the presently claimed compounds, a xanthone moiety would function as a dye. The Examiner does not point to such a disclosure in the Abrahart reference. In fact, it is *not* true that the compounds of the invention are dyes. The inventors have informed the undersigned that the compounds of the invention exhibit very pale colors. For example, an aqueous solution of the compound in Example I in the specification (concentration about 1 ppm = 1 mg/ml) is almost colorless. Because the compounds of the invention do not function as dyes, there would have been no motivation, with a reasonable expectation of success, for a skilled worker to replace any of the substituents on the benzyl ring of the xanthone moiety of a compound of the invention with an auxochrome.

Furthermore, the Examiner has provided no motivation to substitute the claimed compounds with the *particular* groups which are present in the terminal benzene ring of the xanthone moiety of Xanthofulvin or its tautomer in a compound of the invention. For example, the Examiner has provided no motivation to substitute COOH for OH, or OH for H, at the indicated positions or, as is shown in the figure on page 19, at *different* positions in the terminal side of the tricyclic (xanthone) moiety. Absent such motivation, with a reasonable expectation of success, the combination of references does not render the present claims obvious.

As stated above, Xanthofulvin and its tautomer are never included in the scope of claim 1 of the present application. Masubichi *et al.* does not suggest or disclose the claimed compounds; and the secondary reference, Abrahart, does not remedy this deficiency. The combination of the cited references does not render the presently claimed compounds obvious.

Reconsideration and withdrawal of the rejection is requested.


#### Double patenting rejection

Applicants request that this rejection be held in abeyance until there is clearly allowed subject matter.

In view of the preceding arguments, Applicants believe that the claims are in condition for allowance, which action is respectfully requested.

Respectfully submitted,

Date: March 4, 2009

A handwritten signature in black ink, appearing to read "Nancy Axelrod", is written over a horizontal line.

Nancy Axelrod, Ph.D.

Registration No. 44,014

VENABLE

P.O. Box 34385

Washington, D.C. 20043-9998

Telephone: (202) 344-4000

Telefax: (202) 344-8300

DC2/1018295